

Claims

1. A composition comprising
an immunostimulatory nucleic acid molecule comprising the nucleotide sequence of
SEQ ID NO:1.

5

2. The composition of claim 1, wherein the immunostimulatory nucleic acid
molecule consists of the nucleotide sequence of SEQ ID NO:1.

3. The composition of claim 1, further comprising an antigen.

10

4. The composition of claim 3, wherein the antigen is selected from the group
consisting of a microbial antigen, a cancer antigen, and an allergen.

5. The composition of claim 4, wherein the microbial antigen is selected from the
group consisting of a bacterial antigen, a viral antigen, a fungal antigen and a parasitic
antigen.

15

6. The composition of claim 3, wherein the antigen is encoded by a nucleic acid
vector.

20

7. The composition of claim 3, wherein the nucleic acid vector is separate from
the immunostimulatory nucleic acid.

8. The composition of claim 3, wherein the antigen is a peptide antigen.

25

9. The composition of claim 1, further comprising an adjuvant.

10. The composition of claim 9, wherein the adjuvant is a mucosal adjuvant.

11. The composition of claim 1, further comprising a cytokine.

30

12. The composition of claim 1, further comprising a therapeutic agent selected from the group consisting of an anti-microbial agent, an anti-cancer agent, an allergy/asthma medicament.

5 13. The composition of claim 12, wherein the anti-microbial agent is selected from the group consisting of an anti-bacterial agent, an anti-viral agent, an anti-fungal agent, and an anti-parasite agent.

10 14. The composition of claim 12, wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a cancer vaccine, and an immunotherapeutic agent.

15 15. The composition of claim 12, wherein the allergy/asthma medicament is selected from the group consisting of PDE-4 inhibitor, bronchodilator/beta-2 agonist, K⁺ channel opener, VLA-4 antagonist, neurokin antagonist, TXA₂ synthesis inhibitor, xanthanine, arachidonic acid antagonist, 5 lipoxygenase inhibitor, thromboxin A₂ receptor antagonist, thromboxane A₂ antagonist, inhibitor of 5-lipoxygenase activation protein, and protease inhibitor.

20 17. The composition of claim 1, wherein the immunostimulatory nucleic acid has a nucleotide backbone which includes at least one backbone modification.

25 18. The composition of claim 17, wherein the backbone modification is a phosphorothioate modification.

19. The composition of claim 17, wherein the nucleotide backbone is chimeric.

20. The composition of claim 17, wherein the nucleotide backbone is entirely modified.

30 21. The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

22. The composition of claim 1, wherein the immunostimulatory nucleic acid is free of methylated CpG dinucleotides.

5 23. The composition of claim 1, wherein the immunostimulatory nucleic acid includes at least four CpG motifs.

24. The composition of claim 1, wherein the immunostimulatory nucleic acid is T-rich.

10

25. The composition of claim 1, wherein the immunostimulatory nucleic acid includes a poly-T sequence.

15 26. The composition of claim 1, wherein the immunostimulatory nucleic acid includes a poly-G sequence.

27. The composition of claim 1, wherein the immunostimulatory nucleic acid is formulated for oral administration.

20 28. The composition of claim 1, wherein the immunostimulatory nucleic acid is formulated as a nutritional supplement.

29. The composition of claim 28, wherein the nutritional supplement is formulated as a capsule, a pill, or a sublingual tablet.

25

30. The composition of claim 1, wherein the immunostimulatory nucleic acid is formulated for local administration.

30 31. The composition of claim 1, wherein the immunostimulatory nucleic acid is formulated for parenteral administration.

32. The composition of claim 1, wherein the immunostimulatory nucleic acid is formulated in a sustained release device.

33. The composition of claim 1, wherein the immunostimulatory nucleic acid is formulated for delivery to a mucosal surface.

34. The composition of claim 1, wherein the mucosal surface is selected from the group consisting of an oral, nasal, rectal, vaginal, and ocular surface.

35. The composition of claim 1, wherein the immunostimulatory nucleic acid stimulates a mucosal immune response.

36. The composition of claim 1, wherein the immunostimulatory nucleic acid stimulates a systemic immune response.

37. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to stimulate a mucosal immune response.

38. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to stimulate a systemic immune response.

39. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to stimulate an innate immune response.

40. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to treat or prevent an infectious disease.

41. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to treat or prevent an allergy.

42. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to treat or prevent asthma.

43. The composition of claim 1, wherein the immunostimulatory nucleic acid is provided in an amount effective to treat or prevent a cancer.

5 44. The composition of claim 32, wherein the sustained release device is a microparticle.

45. The composition of claim 40, wherein the infectious disease is a herpes simplex virus infection.

10 46. A method for stimulating an immune response in a subject in need thereof comprising administering to a subject an immunostimulatory nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, in an amount effective to stimulate an immune response.

47. The method of claim 46, wherein the subject has or is at risk of developing an infection.

20 48. The method of claim 47, wherein the infection is selected from the group consisting of a bacterial infection, a viral infection, a fungal infection, and a parasite infection.

25 49. The method of claim 48, wherein the viral infection is selected from the group consisting of Human immunodeficiency viruses (HIV-1 and HIV-2), Human T lymphotropic virus type I (HTLV-I), Human T lymphotropic virus type II (HTLV-II), Herpes simplex virus type I (HSV-1) Herpes simplex virus type 2 (HSV-2), Human papilloma virus (multiple types), Hepatitis A virus, Hepatitis B virus, Hepatitis C and D viruses, Epstein-Barr virus (EBV), Cytomegalovirus and Molluscum contagiosum virus.

30 50. The method of claim 49, wherein the viral infection is a herpes simplex virus infection.

51. The method of claim 46, wherein the subject has or is at risk of developing allergy.

5 52. The method of claim 46, wherein the subject has or is at risk of developing asthma.

53. The method of claim 46, wherein the subject has or is at risk of developing a cancer.

10 54. The method of claim 46, further comprising administering an antigen to the subject.

55. The method of claim 53, wherein the antigen is selected from the group consisting of a microbial antigen, a cancer antigen, a self antigen, and an allergen.

15 56. The method of claim 54, wherein the microbial antigen is selected from the group consisting of a bacterial antigen, a viral antigen, a fungal antigen, and a parasitic antigen.

20 57. The method of claim 55, wherein the antigen is derived from a microorganism selected from the group consisting of herpesviridae, retroviridae, orthomyxoviridae, toxoplasma, haemophilus, campylobacter, clostridium, E.coli, and staphylococcus.

25 58. The method of claim 46, wherein the immune response is an antigen-specific immune response.

59. The method of claim 53, wherein the antigen is encoded by a nucleic acid vector.

30 60. The method of claim 59, wherein the nucleic acid vector is separate from the immunostimulatory nucleic acid.

61. The method of claim 54, wherein the antigen is a peptide antigen.

62. The method of claim 46, further comprising administering an adjuvant to the subject.

5

63. The method of claim 62, wherein the adjuvant is a mucosal adjuvant.

64. The method of claim 46, further comprising administering to the subject a second therapeutic agent.

10

65. The method of claim 64, wherein the second therapeutic agent is an anti-microbial agent.

66. The method of claim 65, wherein the anti-microbial agent is selected from the group consisting of an anti-bacterial agent, an anti-viral agent, an anti-fungal agent, and an anti-parasite agent.

15

67. The method of claim 64, wherein the second therapeutic agent is an anti-cancer agent.

20

68. The method of claim 67, wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a cancer vaccine, and an immunomodulatory agent.

25

69. The method of claim 64, wherein the second therapeutic agent is an allergy/asthma medicament.

70. The method of claim 69, wherein the allergy/asthma medicament is selected from the group consisting of PDE-4 inhibitor, bronchodilator/beta-2 agonist, K⁺ channel opener, VLA-4 antagonist, neurokin antagonist, TXA₂ synthesis inhibitor, xanthanine, arachidonic acid antagonist, 5 lipoxygenase inhibitor, thromboxin A₂ receptor antagonist, thromboxane A₂ antagonist, inhibitor of 5-lipoxygenase activation protein, and protease inhibitor.

30

71. The method of claim 46, wherein the immunostimulatory nucleic acid has a nucleotide backbone which includes at least one backbone modification.

5 72. The method of claim 71, wherein the backbone modification is a phosphorothioate modification.

73. The method of claim 71, wherein the nucleotide backbone is chimeric.

10 74. The method of claim 71, wherein the nucleotide backbone is entirely modified.

75. The method of claim 46, wherein the immunostimulatory nucleic acid is free of methylated CpG dinucleotides.

15 76. The method of claim 46, wherein the immunostimulatory nucleic acid includes a poly-G sequence.

77. The method of claim 46, wherein the immunostimulatory nucleic acid is administered orally.

20 78. The method of claim 46, wherein the immunostimulatory nucleic acid is administered locally.

25 79. The method of claim 46, wherein the immunostimulatory nucleic acid is administered parenterally.

80. The method of claim 46, wherein the immunostimulatory nucleic acid is administered in a sustained release device.

30 81. The method of claim 46, wherein the immunostimulatory nucleic acid is administered to a mucosal surface.

82. The method of claim 46, wherein the immune response is a mucosal immune response.

83. The method of claim 46, wherein the immune response is a systemic immune response.

84. The method of claim 81, wherein the mucosal surface is selected from the group consisting of an oral, nasal, rectal, vaginal, and ocular surface.

85. The method of claim 46, further comprising isolating an immune cell from the subject, contacting the immune cell with an effective amount to activate the immune cell of the immunostimulatory nucleic acid and re-administering the activated immune cell to the subject.

86. The method of claim 85, wherein the immune cell is a leukocyte.

87. The method of claim 85, wherein the immune cell is a dendritic cell.

88. The method of claim 85, further comprising contacting the immune cell with an antigen.

89. The method of claim 46, wherein the subject is a human.

90. The method of claim 46, wherein the subject is selected from the group consisting of a dog, cat, horse, cow, pig, sheep, goat, chicken, monkey and fish.

91. The method of claim 46, wherein the subject has or is at risk of developing an infectious disease and wherein the method is a method for treating or preventing the infectious disease.

92. The method of claim 46, wherein the subject has or is at risk of developing asthma and the method is a method of treating or preventing asthma in the subject.

93. The method of claim 46, wherein the subject has or is at risk of developing allergy and the method is a method of treating or preventing allergy.

5 94. The method of claim 46, wherein the subject has or is at risk of developing a cancer and the method is a method of treating or preventing the cancer.

95. The method of claim 94, wherein the cancer is selected from the group consisting of biliary tract cancer; bone cancer; brain and CNS cancer; breast cancer; cervical
10 cancer; choriocarcinoma; colon cancer; connective tissue cancer; endometrial cancer; esophageal cancer; eye cancer; gastric cancer; Hodgkin's lymphoma; intraepithelial neoplasms; larynx cancer; lymphomas; liver cancer; lung cancer (e.g. small cell and non-small cell); melanoma; neuroblastomas; oral cavity cancer; ovarian cancer; pancreas cancer; prostate cancer; rectal cancer; sarcomas; skin cancer; testicular cancer; thyroid cancer;
15 and renal cancer.

96. The method of claim 46, further comprising administering an antibody specific for a cell surface antigen, and wherein the immune response results in antigen dependent cellular cytotoxicity (ADCC).

20

97. A method for preventing disease in a subject, comprising administering to the subject an immunostimulatory nucleic acid on a regular basis to prevent disease in the subject, wherein the immunostimulatory nucleic acid has a nucleotide sequence comprising SEQ ID NO:1.

25

98. A method for inducing an innate immune response, comprising administering to the subject an immunostimulatory nucleic acid in an amount effective for activating an innate immune response, wherein the immunostimulatory nucleic acid has a nucleotide sequence comprising SEQ ID NO:1.

30

99. A method for identifying an immunostimulatory nucleic acid comprising

measuring a control level of activation of an immune cell population contacted with an immunostimulatory nucleic acid comprising a nucleotide sequence of SEQ ID NO:1,

measuring a test level of activation of an immune cell population contacted with a test nucleic acid, and

5 comparing the control level of activation to the test level of activation,
wherein a test level that is equal to or above the control level is indicative of an immunostimulatory nucleic acid.